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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/716,028	11/17/00	LOWMAN	H P1123R1D1

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HM22/0503

EXAMINER	
EWOLDT,G	
ART UNIT	PAPER NUMBER
1644	5

DATE MAILED: 05/03/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/716,028	Lowman et al.
Examiner	**Art Unit**
G. R. Ewoldt	1644

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Nov 17, 2000*.

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *32-41* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *32-41* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☐ Notice of References Cited (PTO-892)

16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____

18) ☐ Interview Summary (PTO-413) Paper No(s). _____

19) ☐ Notice of Informal Patent Application (PTO-152)

20) ☐ Other:

DETAILED ACTION

1. The reference in the first line of the specification must be updated to indicate that the instant application is a divisional application of parent application 09/109,207, now U.S. Patent No. 6,172,213.

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 32-41 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims. While being enabling for:

a composition of an improved anti-IgE binding fragment in combination with an adjunct immunosuppressive agent comprising SEQ ID NOS:15 and 16 (e26), or SEQ ID NOS:17 and 18 (e27),

the specification does not reasonably provide enablement for:

a composition of an improved anti-IgE binding fragment in combination with an adjunct immunosuppressive agent comprising an anti-IgE antibody or IgE binding fragment that has at least one replaced aspartyl residue prone to isomerization replaced while retaining at least the same or greater affinity for IgE than the corresponding unimproved antibody or IgE binding fragment.

Tables 1-9 and 15-18 disclose numerous clones and constructs that were prepared in an attempt to produce the claimed invention. Of the clones with the claimed limitation of a mutated aspartyl residue, only the e26 and e27 constructs function as claimed. The specification provides insufficient guidance in regard to how to prepare the binding proteins of the claimed invention other than by trial and error. Trial and error approaches alone, however, provide an insufficient expectation of success (as demonstrated by the numerous constructs disclosed in the specification that do not function as claimed) and are thus

considered to be highly unpredictable and requiring of undue experimentation.

In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. Thus, in view of the quantity of experimentation necessary, the lack of working examples other than e26 and e27, the unpredictability of the art, and the lack of sufficient guidance in the specification regarding both how to make the claimed invention, it would take undue trials and errors to practice the invention of the instant claims.

4. Claims 32-41 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

There is insufficient written description to show that Applicant was in possession of:

A) a composition of an improved anti-IgE binding fragment in combination with an adjunct immunosuppressive agent comprising an anti-IgE antibody or IgE binding fragment that has at least one replaced aspartyl residue prone to isomerization replaced while retaining at least the same or greater affinity for IgE than the corresponding unimproved antibody or IgE binding fragment, other than e26 or e27 (Claim 32),

B) an immunosuppressive agent comprising an anti-idiotypic antibody which bind MHC antigens or fragments (Claim 34),

C) an immunosuppressive agent comprising cytokine or cytokine receptor antagonists,

D) an immunosuppressive agent comprising anti-lymphocyte globulin (Claim 35),

E) an immunosuppressive agent comprising a soluble peptide containing a LFA-3 binding domain (Claim 36),

F) an immunosuppressive agent comprising a T cell receptor (Claim 36),

G) an immunosuppressive agent comprising T cell receptor antibodies (Claim 36).

Regarding A), the specification discloses only the species e26 and e27, while Claim 32 recites an entire genus. Said genus, however, has not been demonstrated to exist and thus cannot be adequately described. As such, one of skill in the art would conclude that the specification fails to disclose a representative number of species to describe the claimed genus.

Regarding B-F), the "immunosuppressive agents" of the claims are all subgenuses of the immunosuppressive agent genus. However, no species, or actual specific agents are disclosed. As such, one of skill in the art would again conclude that the specification fails to disclose a representative number of species to describe the claimed subgenuses. See *Eli Lilly*, 119 F.3d 1559, 43 USPQ2d 1398.

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 33-36 and 40 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically:

A) In claim 33, the combination of a subgenus, i.e., "2-amino-5-aryl-substituted pyrimidines", and multiple species, i.e., "azathioprine" etc., comprises an improper Markush grouping, thus the claim is indefinite,

B) In claim 34, the combination of multiple subgenuses, i.e., "anti-idiotypic antibodies" etc., and multiple species, i.e., "cyclosporin A" etc., comprises an improper Markush grouping, thus the claim is indefinite,

C) In claim 35, the combination of a genus, i.e., "antibodies" etc., and a species, i.e., "anti-CD3" etc., comprises an improper Markush grouping, thus the claim is indefinite,

D) In claim 33, the combination of multiple subgenuses, i.e., "T cell receptor antibodies" etc., and a species, i.e., "streptokinase" etc., comprises an improper Markush grouping, thus the claim is indefinite,

E) In claim 34, the absence of the word "of" after "consisting" renders the claim nonsensical and thus indefinite,

F) In claim 35, "anti-lymphocyte globulin" has not been defined in the specification, thus the metes and bounds of the claim are unclear and indefinite,

G) Claims 35 and 36 are nonsensical, and thus indefinite, in that the members of the "antibody" Markush groupings do not comprise antibodies,

G) Claim 40 is a reiteration of Claim 37.

7. No claim is allowed.

8. Compositions comprising SEQ ID NOS:15-26 and an immunosuppressive agent appear to be free of the prior art.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Gerald Ewoldt whose telephone number is (703) 308-9805. The examiner can normally be reached Monday through Thursday and alternate Fridays from 7:30 am to 5:30 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

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April 30, 2001

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